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## ORIGINAL ARTICLE

# Increasing awareness and knowledge of lifestyle recommendations for cancer prevention in Lynch syndrome carriers: Randomized controlled trial

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Lynch syndrome (LS) mutation carriers may reduce their cancer risk by adhering to lifestyle recommendations for cancer prevention. This study tested the effect of providing LS mutation carriers with World Cancer Research Fund-the Netherlands (WCRF-NL) health promotion materials on awareness and knowledge of and adherence to these recommendations. In this randomized controlled trial ( $n = 226$ ), the intervention group ( $n = 114$ ) received WCRF-NL health promotion materials. All LS mutation carriers were asked to fill out questionnaires at 2 weeks before (baseline, T0) and at 2 weeks (T1) and 6 months (T2) after the intervention. Linear mixed models were performed on awareness (0-7) and knowledge (0-7) of the recommendations, and on the secondary outcomes, that is adherence, distress, cancer worry, and risk perception. Compared with the control group, the intervention group became significantly more aware (overall mean difference = 1.24; 95%CI = 0.82-1.67) and obtained significantly improved knowledge of the recommendations (overall mean difference = 1.65; 95%CI = 1.27-2.03). Differences were significantly larger for T1 ( $P_{\text{interaction}} = .003$  and  $\leq .001$ , respectively) but remained significant for T2. No effect on secondary outcomes was found. In conclusion, provision of WCRF-NL health promotion materials increases awareness and knowledge of lifestyle recommendations for cancer prevention among LS mutation carriers without causing additional distress, but does not affect adherence.

## KEYWORDS

adherence, awareness, cancer prevention, health education and promotion, intervention, lifestyle recommendation, Lynch syndrome

## 1 | INTRODUCTION

Lynch syndrome (LS) is a dominantly inherited syndrome characterized by a high risk of colorectal cancer (CRC), endometrial cancer and other types of cancer relatively early in life.<sup>1-6</sup> Risk of developing CRC up to age 70 in LS is 22%-69%,<sup>1-4</sup> as compared with 1%-5% in the general Western population.<sup>7</sup> The syndrome is caused by

germline mutations in genes involved in or influencing DNA mismatch repair (MMR): *MLH1*, *MSH2*, *MSH6* and *PMS2* or a 3' deletion of *EPCAM*.<sup>8,9</sup> Clinical expression of LS varies worldwide.<sup>10</sup> Moreover, risk of CRC varies in and between families.<sup>11</sup> Possible explanations for these differences are influences of modifier genes<sup>12</sup> and dietary or other lifestyle factors.

Numerous studies have investigated the association between dietary intake and other lifestyle factors and sporadic CRC.<sup>13</sup> There is general agreement that smoking, higher body fatness, abdominal fatness, red meat and processed meat intake, and lower dietary fiber

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intake and insufficient physical activity are associated with higher CRC risk. In addition, higher alcohol intake is associated with higher CRC risk in men, and probably also in women. Moreover, there is limited suggestive evidence for a protective effect of non-starchy vegetables and fruit.<sup>14</sup> Only few studies evaluated the association between dietary and other lifestyle factors and cancer risk in LS mutation carriers.<sup>15</sup> These studies suggested that the association of smoking and higher body fatness with CRC risk was in the same direction and generally stronger in LS mutation carriers than in the general population.<sup>15</sup> Other lifestyle factors have not yet or only scarcely been studied.

On the basis of the most comprehensive collection of available evidence on sporadic cancer, the World Cancer Research Fund (WCRF)/American Institute of Cancer Research (AICR) issued 10 general recommendations on diet, physical activity, breast feeding and weight management for cancer prevention,<sup>13</sup> besides the recommendation to quit smoking. Little is known about the extent to which LS mutation carriers are aware of and adhere to these lifestyle recommendations.

Currently, guidelines for clinicians do not include information on these lifestyle recommendations for potential health benefits for LS mutation carriers.<sup>16,17</sup> Providing health promotion materials could be an easy-to implement approach to promote awareness and knowledge (ie, known determinants of adherence) in LS mutation carriers. This may subsequently promote adherence to lifestyle recommendations, leading to potential health benefits. The aim of this randomized controlled study was to test the effect of providing LS mutation carriers with WCRF-NL health promotion materials on awareness and knowledge of the WCRF/AICR cancer prevention recommendations. In addition, we tested the effect of providing these WCRF-NL health promotion materials on adherence to these recommendations and on levels of distress, cancer worry and cancer risk perception.

## 2 | METHODS

The medical ethical research committees of the Radboud university medical center and Maastricht University Medical Centre granted permission to perform this study.

### 2.1 | Participants and study procedures

LS mutation carriers were eligible for participation in this study if mutation status was confirmed by DNA testing and carriers were informed about the LS carriership at Radboud or Maastricht University Medical Center within the last 6 years, and were aged between 18 and 65 years at the time of inclusion in the study between April and September 2015. LS mutations carriers were excluded if they had insufficient command of the Dutch language to fill out Dutch questionnaires or if they were currently participating in the GeoLynch study, a prospective cohort study among LS mutation carriers,<sup>18</sup> to prevent interference between both studies.

After informed consent was obtained, eligible participants were randomized into an intervention or control group (Figure 1). To minimize the risk of interference between family members, randomization was performed per family in clusters.

### 2.2 | Intervention

The intervention group received WCRF-NL health promotion materials about lifestyle recommendations for cancer prevention. The WCRF materials included 1 general leaflet, which provided information about cancer development, cancer prevention and the 10 WCRF/AICR cancer prevention recommendations: (1) Be as lean as possible without becoming underweight, (2) be physically active for at least 30 minutes every day, (3) limit consumption of energy-dense foods and avoid sugary drinks, (4) eat more of a variety of vegetables, fruits, whole grains and legumes such as beans, (5) limit consumption of red meats (such as beef, pork and lamb) and avoid processed meats if consumed at all, (6) limit alcoholic drinks to 2 for men and 1 for women a day, (7) limit consumption of salty foods and foods processed with salt (sodium), (8) don't rely on supplements to protect against cancer, (9) it is best for mothers to breastfeed exclusively for up to 6 months, and (10) after treatment, cancer survivors should follow the recommendations for cancer prevention.

The other leaflet provided specific information about CRC: CRC development, symptoms, risk factors, and the lifestyle recommendations that have been related to a reduced risk of CRC. A reference to the website of the WCRF was included for additional information.

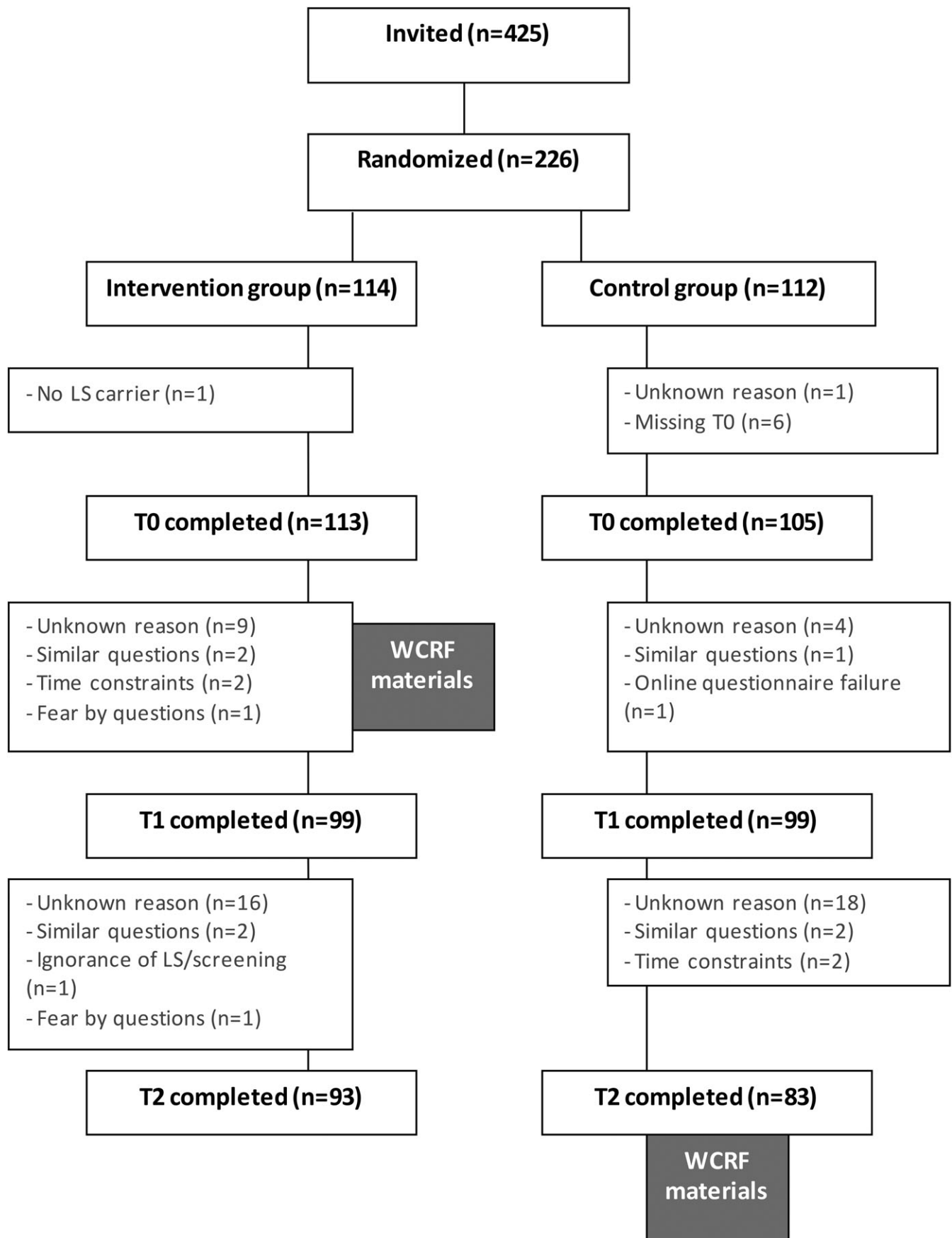
The control group did not receive any information during the study period but received the same leaflets after completing the last questionnaire.

### 2.3 | Study outcomes

Participants filled out questionnaires at 3 time points: 2 weeks before the intervention (T0) and at 2 weeks (T1) and 6 months (T2) after the intervention, either online or on paper. These questionnaires measured the following parameters.

#### 2.3.1 | Primary outcomes

*Awareness of the cancer risk factors as described in the WCRF/AICR recommendations for cancer prevention* (referred to as awareness of the WCRF/AICR recommendations) was measured using the question from the AICR Cancer Risk Awareness Survey "Do the following factors have a significant effect on whether or not the average person develops cancer?" with respect to the exposures: (1) overweight, (2) insufficient physical activity, (3) diets low in vegetables and fruits, (4) diets high in red meat, (5) cured/ processed meats, (6) alcohol, and (7) use of food supplements for cancer prevention.<sup>19</sup> Other non-cancer-related factors were added to this list. Correct answers were rated "1," incorrect answers "0." The total awareness score ranged between 0 and 7. In addition, *knowledge of the WCRF/AICR recommendations* was measured using 7 multiple choice questions. In addition to the awareness questionnaire, the knowledge questions included more content-specific topics, for example "What is the minimally recommended fruit and vegetable intake per day according to the recommendations for cancer prevention?". Correct answers were rated "1," incorrect answers "0." The total knowledge score ranged between 0 and 7.



**FIGURE 1** Flowchart of study design and participant flow (CONSORT diagram)

### 2.3.2 | Secondary outcomes

Adherence to the WCRF/AICR recommendations was measured using the WCRF/AICR score, which is based on the WCRF/AICR recommendations.<sup>20</sup> The score we used was a slightly modified version of this score and its construction is shown in Table 1.<sup>20</sup> For some recommendations insufficient data was available, for example, data was missing for food supplement intake, breastfeeding, or consumption of energy dense foods. The score assigned for each recommendation was 1 point when the recommendation was met and 0 points when the recommendation was not met. For some variables, an intermediate category (0.5 points) was created to increase variability in the population. The cut-off values for dietary fiber and sodium were proportionally lowered matching the percentage coverage of total energy intake as assessed by the adapted Dutch Healthy Diet-Food Frequency Questionnaire (DHD-FFQ) (68%). The combined subscores for plant foods, dietary fiber and vegetable and fruit intake, were averaged, as were the subscores for sodium and discretionary sodium. The total WCRF/AICR score ranged between 0 (no adherence) to 7 points (complete adherence).

This score was assessed using the following questionnaires:

1. *Dietary behaviour* was assessed using an adapted version of a 40-item, validated questionnaire (FFQ) specifically developed to assess adherence to the Dutch Guidelines for a healthy diet.<sup>21</sup>

With this questionnaire, we assessed intake of fruits (gram [g]/day [d]), vegetables (g/d), red meat (g/week [w]), processed meat (g/w), drinks that promote weight gain (sugary drinks or no sugary drinks), fiber intake (g/d), alcoholic drinks (number of drinks/d), and discretionary sodium (yes or no) during the last month.<sup>21</sup>

2. *Physical activity* was assessed using the validated Short Questionnaire to Assess Health Enhancing Physical Activity (SQUASH) questionnaire which contains questions about multiple activities referring to a normal week in the past month. Results were converted to time spent in light, moderate, and vigorous activities, which were then converted to activity scores.<sup>22</sup> When this total activity score was 5 or more, representing the number of activities of at least 30 minutes per week, persons were categorized as adherent to the physical activity recommendation.
3. *Anthropometric measurements* included self-reported body weight and height. These measures were used to calculate the body mass index (BMI) (kg/m<sup>2</sup>).

*Cancer risk perception* was assessed by 2 standardized questions.<sup>23</sup> Participants were asked to indicate their cancer risk quantitatively (percentage from 0 to 100) and qualitatively (5 categories: very low to very high).

**TABLE 1** WCRF/AICR recommendations for cancer prevention as operationalized in the WCRF score used

Category	Recommendations	WCRF score		
		0 points	0.5 points	1 point
Body fatness	Maintain body weight within the normal range from age 21	<18.5 or >30 kg/m <sup>2</sup>	25-<30 kg/m <sup>2</sup>	18.5-<25 kg/m <sup>2</sup>
Physical activity	Be moderately physically active, equivalent to brisk walking, for at least 30 minutes every day	<30 min/d	—	>30 min/d
Foods and drinks that promote weight gain	Avoid sugary drinks	Sugary drinks	—	No sugary drinks
Plant foods	Eat at least 5 portions/ servings (at least 400 g) of a variety of non-starchy vegetables of fruits every day	F&V <200 g/d Dietary fiber <8.5 g/d <sup>a</sup>	F&V 200-<400 g/d Dietary fiber 8.5-<17 g/d <sup>a</sup>	F&V ≥400 g/d Dietary fiber ≥17 g/d <sup>a</sup>
Animal foods	People who eat red meat to consume less than 500 g/ wk, very little, if any, to be processed	Red/processed meat ≥500 g/wk of which processed meat ≥50 g/d	Red/processed meat <500 g/wk of which processed meat 3-<50 g/d	Red/processed meat <500 g/wk of which processed meat <3 g/d
Alcoholic drinks	If alcoholic drinks are consumed, limit consumption to no more than 2 drinks a day for men, and 1 drink a day for women	♂: >3 drinks ♀: >2 drinks	♂: 2-≤3 drinks ♀: 1-≤2 drinks	♂: ≤2 drinks ♀: ≤1 drinks
Preservation, processing, preparation	Limit consumption of processed foods with added salt to ensure an intake of less than 6 g (2.4 g sodium) a day	>1632 mg/d <sup>a</sup> Always using discretionary sodium		≤1632 mg/d <sup>a</sup> Never using discretionary sodium

Abbreviations: DHD-FFQ, Dutch Healthy Diet-Food Frequency Questionnaire; WCRF/AICR, World Cancer Research Fund/American Institute of Cancer Research.

<sup>a</sup> Lowered by matching the percentage coverage of total energy intake as assessed by the adapted short version of the DHD-FFQ (68%).

The total score of the Dutch version of the Hospital Anxiety and Depression Scale (HADS)<sup>24</sup> was used to measure *distress*. The questionnaire contained 14 items scored on a 4-point scale with total scores ranging from 0 to 42. A higher total score corresponded with a higher level of distress. A score  $\geq 12$  was appointed as a clinically increased level of distress. This questionnaire has been shown to have good reliability.<sup>24</sup>

*Cancer worry* was assessed using the Cancer Worry Scale (CWS), consisting of 8 items. The reliability and validity is good among breast and colorectal cancer survivors.<sup>25,26</sup> The total score ranges between 8 and 32, with higher scores corresponding to more cancer worry. A cut-off score of 14 is generally accepted for differentiating normal from increased levels of cancer worry.

*Satisfaction with and the use of the WCRF health promotion materials* were measured at T2, using self-developed questions concerning general satisfaction, timing of the intervention, frequency of use of the WCRF health promotion materials, and reasons for non-usage. At T2, both groups were asked whether they searched for additional or other information concerning lifestyle and cancer risk during the study period.

Questions concerning *medical data* (on personal and family cancer history, colon surgery, time since LS diagnosis), and *demographic questions* (age, occupation, marital status and education) were included in the baseline questionnaire.

## 2.4 | Power calculations and statistical analyses

The sample size calculation was based on the primary outcome awareness of the WCRF/AICR recommendations. Estimated effects were based on a study of adolescents assessing the effect of an educational intervention on 11 cancer risk factors.<sup>27</sup> To detect a  $1.1 \pm 2.7$  between-group difference in risk factors, with a 2-sided alpha of .05 and a power of 80%, a total of 200 LS mutation carriers were needed (in case of standard randomization per person). In this cluster randomized design (per family) the expected inter-cluster correlation was 0.05 and the expected average family size was 4 persons, resulting in a total of 230 LS mutation carriers (115 per group).

Descriptive statistics were used to describe participants' demographics at baseline and the satisfaction outcomes. Differences in primary and secondary outcomes between the intervention and the control group were analyzed with linear mixed models, taking into account the repeated measures and family-clustered design. In all analyses, an adjustment was made for the baseline value of the particular outcome. The following analyses were performed: (1) Crude analysis for the overall intervention effect. (2) Crude analysis with time (categorical dummy variable) and an interaction term for time and intervention to assess the intervention effect at T1 and T2. (3) Same analysis as (2) adjusted for the covariates age, gender, level of education, and years since LS diagnosis. For the primary outcomes awareness and knowledge, the same analysis as (3) was performed with an interaction term for the covariates [age less than or greater than or equal to median of 49 years, gender, level of education (low vs middle and high) and years since LS diagnosis less than or greater than or equal to median of 3 years] and intervention to assess whether the intervention effect differed for the subgroups.

Additionally, analyses were performed separately for participants with vs without a personal history of cancer, completing questionnaires online vs on paper, and with baseline WCRF adherence scores  $<5$  vs  $\geq 5$ . Differences in awareness and knowledge of and adherence to the individual WCRF/AICR recommendations between the intervention and the control group were analyzed with generalized estimation equations using a logistic model, taking into account the repeated measures but not the family-clustered design (no significant cluster effect in linear mixed models analyses). We performed (1) a crude analysis for the overall intervention effect and (2) a crude analysis with time (categorical dummy variable) and an interaction term for time and intervention to assess the intervention effect at T1 and T2. All analyses were carried out according to modified intention-to-treat (mITT) methodology. mITT allows the exclusion of some randomized subjects in a justified way (such as subjects who were deemed ineligible after randomization or certain subjects of whom all measurements were missing).<sup>28</sup> All reasons for exclusions after randomization are shown in Figure 1. All the analyses were performed using IBM SPSS, version 22 and  $P < .05$  was considered statistically significant.

## 3 | RESULTS

We invited 425 LS mutation carriers and 226 agreed to participate (response rate 53%). In total, 114 carriers (from 62 families) were randomized to the intervention group and 112 carriers (from 62 families) to the control group. Reasons for exclusion after randomization are described in Figure 1, leaving a total of 218 LS mutation carriers for analysis. Patient characteristics are shown in Table 2. The percentage of higher educated persons and never smokers was higher in the intervention group compared with the control group. Other than that, characteristics were similar for the intervention and control group. A total of 35% of the study population reported a personal history of cancer.

As shown in Table 3, awareness was significantly higher in the intervention group compared with the control group (mean difference = 1.24; 95% CI = 0.82-1.67). The difference in awareness was larger for T1 but remained significant for T2 (mean difference = 1.60; 95% CI = 1.12-2.08 and mean difference = 0.82; 95% CI = 0.31-1.33, respectively;  $P_{\text{interaction}} = .003$ ). Adjustment for age, sex, education level, and time since LS diagnosis did not importantly change the results, and no significant interaction with these variables was observed. Also, knowledge was significantly higher in the intervention group compared with the control group (mean difference = 1.65; 95% CI = 1.27-2.03). This difference was also larger for T1 but remained significant for T2 (mean difference = 2.13; 95% CI = 1.70-2.55 and mean difference = 1.12; 95% CI = 0.67-1.56, respectively;  $P_{\text{interaction}} < .001$ ). Adjustment for age, sex, education level, and time since LS diagnosis did not importantly change the results, but a significant interaction with education level was observed. LS mutation carriers with a medium or high education level had a larger overall difference in awareness after intervention than those with a low education level (mean difference = 1.69; 95% CI = 1.30-2.08 and mean difference = 0.40; 95% CI = -0.79 to 1.59, respectively;  $P_{\text{interaction}} = .04$ ; data not shown). No differences in adherence, distress and



**TABLE 2** Baseline demographic and clinical characteristics of the participants

	Intervention (n = 113)	Control (n = 105)
Age	48.6 ± 11.2	47.7 ± 10.6
Gender		
Male	45 (39.8%)	39 (37.1%)
Female	68 (60.2%)	66 (62.9%)
Education		
Low	9 (8.0%)	13 (12.4%)
Medium	55 (48.7%)	56 (53.3%)
High	49 (43.3%)	36 (34.3%)
Employment		
Paid work	81 (71.7%)	74 (70.5%)
No paid work	23 (20.4%)	24 (22.9%)
Retired	9 (8.0%)	7 (6.7%)
Marital status		
Married/civil partnership/ cohabiting	95 (84.1%)	89 (84.8%)
Divorced/Widow/Single	18 (15.9%)	16 (15.2%)
Years since LS diagnosis	3.6 ± 2.5	3.7 ± 2.8
Time since last colonoscopy (months) <sup>a</sup>	14.4 ± 12.3	14.0 ± 11.1
Personal history of cancer		
Yes	44 (38.9%)	33 (31.4%)
No	69 (61.1%)	72 (68.6%)
Colon cancer		
Yes	23 (20.4%)	17 (16.2%)
No	90 (79.6%)	88 (83.8%)
Rectum cancer		
Yes	1 (0.9%)	2 (1.9%)
No	112 (99.1%)	103 (98.1%)
Other type of cancer		
Yes	28 (24.8%)	19 (18.1%)
No	85 (75.2%)	86 (81.9%)
Colon surgery		
Colectomy	5 (4.4%)	2 (1.9%)
Hemicolectomy	14 (12.4%)	11 (10.5%)
Colon resection	3 (2.7%)	4 (3.8%)
Stoma		
Yes	1 (0.9%)	1 (1.0%)
No	112 (99.1%)	104 (99.0%)
First degree family member affected by colon cancer		
Yes	60 (53.1%)	43 (41.0%)
No	53 (46.9%)	62 (59.0%)
Smoking		
Current	10 (8.8%)	13 (12.4%)
Former	45 (39.8%)	51 (48.6%)
Never	58 (51.3%)	41 (39.0%)

Data are reported as the mean ± SD or n (%).

<sup>a</sup> Missing for n = 48 in intervention group and n = 9 in control group.

cancer worry were observed, but perceived cancer risk was significantly lower in the intervention group compared with the control group (mean difference = -4.72; 95% CI = -9.4 to -.05).

When analyses were performed for LS mutation carriers with and without a personal history of cancer, separately, results were very similar for both groups (Tables S1 and S2, Supporting Information). While knowledge increased in both groups, a larger difference in knowledge was found for those with a personal history of cancer (mean difference = 2.12; 95% CI = 1.49-2.74) vs those without (mean difference = 1.39; 95% CI = 0.88-1.80),  $P_{\text{interaction}} = .049$ . Awareness and knowledge did not differ by mode of completing the questionnaire (online for n = 152, on paper for n = 66) and by baseline WCRF adherence score (score <5 for n = 97; score ≥5 for n = 121) (data not shown).

The awareness and knowledge of the WCRF/AICR recommendations varied per recommendation, and was significantly higher for all recommendations in the intervention group compared with the control group at T1 (Table 4). At T2, awareness of the recommendations on food supplements, overweight, and alcohol was no longer significantly higher for the intervention group compared with the control group. Also knowledge of the recommendations on overweight, fruit and vegetables, and red meat was no longer significantly different at T2. After intervention, generally over 80% of the intervention group was aware of the recommendations, except for the recommendation on food supplements (range 40%-50%). Over 80% of the intervention group also had knowledge of the recommendations on overweight, alcohol, and physical activity after the intervention, while knowledge of the other recommendations was lower (range 27%-63%). Adherence to the WCRF/AICR recommendations did not differ between the intervention group and the control group. Highest adherence rates were found for the recommendations on alcohol intake, sugary drink intake, and physical activity (range 73%-93%). Less than half of the LS mutation carriers adhered to the recommendations on BMI and red and processed meat intake while recommendations on fruit, vegetable and dietary fiber intake were followed by only few LS mutation carriers (≤8%).

With regard to usage of the health promotion materials, 90% of the intervention group who completed T1 reported having read the information at least once at T1. Lack of time was the most commonly reported reason for non-usage (5%). The mean patient satisfaction with the health promotion materials was 4.2 ± 0.7 on a 5-point scale. Concerning the timing of the intervention, 46% indicated a preference for receiving the information in an earlier stage after LS diagnosis. After having read the information, at least one self-reported change in lifestyle was made by 50% of the intervention group. Dietary changes were most often reported (35%). During the study period, 41% of the intervention group and 25% of the control group searched for or received additional information on this topic. Table S3 shows the used sources of information. Twenty-seven percent of the intervention group and 41% of the control group expressed a need for support to adhere to the lifestyle recommendations. Preferences of type of support are shown in Table S3.

## 4 | DISCUSSION AND CONCLUSIONS

This is the first study among LS mutation carriers reporting on the effect of health promotion materials for cancer prevention. We

**TABLE 3** Linear mixed model analyses on mean scores of primary and secondary outcomes in intervention and control group

	T0			T1			T2			Crude Overall	P interaction with time	Crude <sup>a</sup>		Adjusted <sup>b</sup>	
	Mean	SD		Mean	SD		Mean	SD		Effect (95% CI)		Time 1 Effect (95% CI)	Time 2 Effect (95% CI)	Time 1 Effect (95% CI)	Time 2 Effect (95% CI)
Awareness total score (0-7)										1.24 (0.82 to 1.67) <sup>c</sup>	0.003	1.60 (1.12 to 2.08) <sup>c</sup>	0.82 (0.31 to 1.33) <sup>d</sup>	1.54 (1.07 to 2.01) <sup>c</sup>	0.73 (0.23 to 1.22) <sup>d</sup>
Intervention	4.02	± 2.04		5.84	± 1.57		5.52	± 1.67							
Control	3.90	± 2.24		4.24	± 2.30		4.64	± 2.22							
Knowledge total score (0-7)										1.65 (1.27 to 2.03) <sup>c</sup>	<0.001	2.13 (1.70 to 2.55) <sup>c</sup>	1.12 (0.67 to 1.56) <sup>c</sup>	2.07 (1.66 to 2.49) <sup>c</sup>	1.04 (0.61 to 1.48) <sup>c</sup>
Intervention	2.18	± 1.49		4.65	± 1.75		3.88	± 1.43							
Control	2.13	± 1.45		2.55	± 1.56		2.71	± 1.61							
WCRF adherence score (0-7)										-0.11 (to 0.30 to 0.09)	0.50	-0.16 (-0.40 to 0.08)	-0.05 (-0.31 to 0.20)	-0.17 (-0.41 to 0.06)	-0.08 (-0.33 to 0.17)
Intervention	4.90	± 0.91		4.87	± 1.00		5.04	± 0.87							
Control	4.77	± 0.82		4.98	± 0.84		5.07	± 0.86							
Distress (HADS-total)										-0.06 (-0.88 to 0.75)	0.12	-0.44 (-1.39 to 0.50)	0.39 (-0.60 to 1.38)	-0.41 (-1.36 to 0.54)	0.43 (-0.57 to 1.43)
Intervention	7.17	± 6.03		6.53	± 5.60		6.85	± 6.03							
Control	7.45	± 7.20		7.09	± 6.98		7.04	± 6.68							
Cancer worry (CWS)										-0.3 (-0.9 to 0.2)	0.64	-0.4 (-1.0 to 0.2)	-0.2 (-0.9 to 0.4)	-0.4 (-1.1 to 0.2)	-0.3 (-1.0 to 0.4)
Intervention	13.7	± 3.8		12.9	± 3.6		12.8	± 3.8							
Control	14.1	± 4.6		13.5	± 4.9		13.5	± 5.0							
Perceived cancer risk (0-100)										-4.7 (-9.4 to -0.1) <sup>e</sup>	0.45	-3.7 (-1.0 to 1.5)	-5.8 (-11 to -0.3) <sup>c</sup>	-3.2 (-8.5 to 2.2)	-5.2 (-10.8 to 0.4)
Intervention	49.4	± 22.9		46.9	± 25.4		44.3	± 23.9							
Control	51.0	± 24.5		51.4	± 26.0		49.8	± 28.4							

<sup>a</sup> Adjusted for score at T0.<sup>b</sup> Adjusted for score at T0 and age, sex, education, and years since LS diagnosis.<sup>c</sup>  $P < .001$  for intervention compared to control group at T1 or T2.<sup>d</sup>  $P < .01$  for intervention compared to control group at T1 or T2.<sup>e</sup>  $P < .05$  for intervention compared to control group at T1 or T2.



**TABLE 4** Generalized estimation equation analyses on scores of awareness, knowledge and adherence scores per component

	T0		T1		T2		P Overall
	Intervention (n = 113)	Control (n = 105)	Intervention (n = 99)	Control (n = 99)	Intervention (n = 93)	Control (n = 83)	
Awareness score components							
Food supplements	33 (29.2%)	31 (29.5%)	49 (49.5%) <sup>a</sup>	36 (36.4%)	38 (40.9%)	32 (38.6%)	0.13
Overweight	83 (73.5%)	74 (70.5%)	93 (93.9%) <sup>c</sup>	76 (76.8%)	80 (86.0%)	65 (61.9%)	0.002
Fruits and vegetables	77 (68.1%)	67 (63.8%)	87 (87.9%) <sup>c</sup>	58 (58.6%)	74 (79.6%) <sup>b</sup>	52 (62.7%)	<0.001
Alcohol	70 (61.9%)	68 (64.8%)	86 (86.9%) <sup>c</sup>	65 (65.7%)	78 (83.9%)	62 (59.0%)	<0.001
Physical activity	75 (66.4%)	69 (65.7%)	92 (92.9%) <sup>c</sup>	69 (69.7%)	80 (86.0%) <sup>c</sup>	54 (65.1%)	<0.001
Red meat	60 (53.1%)	48 (45.7%)	85 (85.9%) <sup>c</sup>	59 (59.6%)	80 (86.0%) <sup>a</sup>	58 (69.9%)	<0.001
Processed meat	56 (49.6%)	53 (50.5%)	86 (86.9%) <sup>c</sup>	57 (57.6%)	83 (89.2%) <sup>b</sup>	62 (74.7%)	<0.001
Knowledge score components							
Food supplements	14 (12.4%)	7 (6.7%)	36 (36.4%) <sup>c</sup>	4 (4.0%)	25 (26.9%) <sup>a</sup>	9 (10.8%)	<0.001
Overweight	60 (53.1%)	54 (51.4%)	85 (85.9%) <sup>c</sup>	65 (61.9%)	72 (77.4%)	56 (68.3%)	0.003
Fruits and vegetables	23 (20.4%)	14 (13.6%)	52 (52.5%) <sup>c</sup>	20 (20.2%)	26 (28.0%)	16 (19.3%)	<0.001
Alcohol	52 (46.0%)	55 (52.4%)	86 (86.9%) <sup>c</sup>	58 (58.6%)	81 (88.0%) <sup>c</sup>	49 (59.0%)	<0.001
Physical activity	72 (63.7%)	68 (64.8%)	87 (87.9%) <sup>b</sup>	71 (71.7%)	81 (87.1%) <sup>b</sup>	60 (73.2%)	0.001
Red meat	15 (13.3%)	15 (14.3%)	52 (52.5%) <sup>c</sup>	18 (18.2%)	26 (28.0%)	18 (21.7%)	<0.001
Processed meat	10 (8.8%)	11 (10.5%)	62 (62.6%) <sup>c</sup>	16 (16.2%)	50 (53.8%) <sup>c</sup>	17 (20.5%)	<0.001
WCRF adherence score components							
BMI	51 (45.1%)	51 (48.6%)	50 (50.5%)	51 (51.5%)	45 (48.4%)	47 (56.6%)	0.96
Physical activity	82 (72.6%)	89 (84.8%)	72 (72.7%)	83 (83.8%)	69 (74.2%) <sup>a</sup>	74 (89.2%)	0.06
Sugary drinks	96 (85.0%)	84 (80.0%)	80 (80.8%)	81 (81.8%)	83 (89.2%)	70 (84.3%)	0.63
F&V and dietary fiber	1 (0.9%)	0 (0.0%)	2 (2.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)	0.60
F&V	5 (4.4%)	5 (4.8%)	4 (4.0%)	3 (3.0%)	4 (4.3%)	1 (1.2%)	0.29
Dietary fiber	7 (6.2%)	8 (7.6%)	8 (8.1%)	4 (3.8%)	6 (6.5%)	7 (8.4%)	0.66
Red and processed meat	45 (39.8%)	28 (26.7%)	39 (39.4%)	41 (41.4%)	42 (45.2%)	31 (37.3%)	0.56
Alcoholic drinks	100 (88.5%)	93 (88.6%)	89 (89.9%)	89 (89.9%)	86 (92.5%)	77 (92.8%)	0.59
Salt intake	61 (54.0%)	46 (43.8%)	54 (54.5%)	54 (54.5%)	56 (60.2%)	40 (48.2%)	0.53

Abbreviations: WCRF, World Cancer Research Fund.

<sup>a</sup>  $P < .05$  for intervention compared with control group at T1 or T2.

<sup>b</sup>  $P < .01$  for intervention compared with control group at T1 or T2.

<sup>c</sup>  $P < .001$  for intervention compared with control group at T1 or T2.

showed that provision of WCRF-NL health promotion materials resulted in increased awareness and knowledge of the lifestyle recommendations for cancer prevention. Although effects remained up to 6 months, they were significantly smaller compared to effects found at 2 weeks after information provision. The provision of information on lifestyle recommendations for cancer prevention did not cause additional distress, cancer worry or a change in risk perception. No effects on adherence to the lifestyle recommendations were found.

Our study population had a relatively high awareness of cancer risk factors at baseline, as compared to the general population.<sup>19,29,30</sup> For example, 72% of our study population was aware of overweight as a cancer risk factor, while this was reported for only 52% of the general population in the US.<sup>19</sup> However, awareness varied by risk factor, with lowest awareness observed for use of food supplements (29%). Specific knowledge of the WCRF/AICR recommendations at baseline (e.g., the recommended intake of processed meat intake per day) was substantially lower than awareness of cancer risk factors, ranging from 10% for processed meat intake and use of food supplements to 64% for physical activity. This is in line with findings from a

representative population sample in the UK, in which 79% knew that eating too much meat increased risk but only 47% and 28% knew the advised amount of red meat and processed meat, respectively.<sup>31</sup> We found that the provision of health promotion materials for cancer prevention improved the awareness and knowledge of all WCRF/AICR recommendations. These improvements remained statistically significant up to 6 months after intervention, although they were statistically significantly smaller than 2 weeks after intervention. Improvements on knowledge were larger for LS mutation carriers with versus without a personal history of cancer, which may be explained by a greater interest in factors that may reduce their (secondary) cancer risk. As expected, awareness and knowledge of the control group remained relatively stable, except for improvements in awareness concerning red meat intake and knowledge concerning body weight. This may be due to media attention with respect to an IARC publication on red meat and cancer risk which occurred after T0, and to searching for additional information on this topic after T0.

The provision of general WCRF-NL health promotion materials did not improve adherence to the WCRF/AICR recommendations for

cancer prevention, as could be expected from previous studies on behaviour changes after provision of other health promotion materials.<sup>32</sup> We observed a large variation in adherence to the different WCRF/AICR recommendations, with hardly any participants adhering to the recommendation for fruit and vegetable intake but more than 80% of participants adhering to the recommendation for sugary drinks. Adherence to the WCRF/AICR recommendations has also been studied among colorectal cancer survivors, who had slightly lower adherence rates compared to our study population.<sup>33</sup> Especially, our study population had higher adherence rates to the red and processed meat recommendations and the recommendation about salt intake. These differences suggest the selection of more health conscious participants in our study, as the study among colorectal cancer survivors was not specifically focused on lifestyle behaviours.<sup>33</sup> Similar to other populations, there is ample room for improvement in adherence among LS mutation carriers.

Awareness and knowledge are known determinants of health behaviour change, and play a key role in numerous health behaviour change theories and models.<sup>34</sup> For example, Prochaska's Transtheoretical model illustrates that increasing awareness or knowledge (e.g., by providing information on WCRF/AICR recommendations) may promote readiness to change lifestyle.<sup>35</sup> In addition, our qualitative study exploring determinants of adherence to the WCRF/AICR recommendations among LS mutation carriers has shown that the Health Belief Model can partly be used to explain adherence to these recommendations in LS mutation carriers.<sup>36</sup> To illustrate, this qualitative study showed that LS mutation carriers perceived receiving information on WCRF/AICR recommendations as a "cue to action" to initiate lifestyle change.

However, our results show that promotion of awareness and knowledge was not sufficient to achieve health behaviour change. These results are in line with other studies, and suggest that a more comprehensive intervention is needed to achieve health behaviour change.<sup>37</sup> Furthermore, our finding that awareness and knowledge of WCRF/AICR recommendations significantly improved from baseline to directly after the provision of health promotion materials, and subsequently decreased at follow-up is in line with scientific literature on lifestyle intervention effects over time.<sup>37</sup> This suggests that offering a more comprehensive lifestyle intervention shortly after provision of health promotion materials may bridge the gap between awareness/knowledge and adherence to recommendations.

To achieve an optimal intervention effect and to promote participation and adherence, a lifestyle intervention offered to LS mutation carriers should meet the needs of this particular patient population. Although we found that patient satisfaction and frequency of use of the provided WCRF-NL materials were high, almost half of the participants indicated a preference to receive the information at an earlier stage after the LS diagnosis. LS mutation carriers may be more open for lifestyle changes sooner after LS diagnosis, as has been observed in studies among cancer survivors.<sup>38</sup> Including LS mutation carriers sooner after diagnosis may increase the effectiveness of this intervention. However, additional analyses in the current trial showed no differences in effect for the small group of LS mutation carriers diagnosed  $\leq 1$  year ( $n = 36$ ) vs. those diagnosed  $>1$  year ago (data not shown).

From the field of health behaviour change, several proven effective behaviour change techniques exist, which may promote adherence.<sup>39</sup> Behaviour change techniques that have shown to be associated with intervention effectiveness include: "social support", "goal setting", action planning", "instruction on how to perform the behaviour", "self-monitoring of behaviour", and "self-monitoring of outcomes of behaviour".<sup>40</sup> Lifestyle interventions that have shown to be effective in promoting adherence are typically more complex and intensive than the minimal intervention we have applied in our study, and make use of a larger amount of behaviour change techniques.<sup>37,40</sup> Therefore, adding such behaviour change techniques to the provision of information on WCRF/AICR recommendations is expected to increase adherence. As lifestyle interventions for LS mutation carriers are not available, we may learn from lifestyle interventions aimed at comparable patient populations, which can be adapted to the needs of LS mutation carriers using the results from this study. Future studies should test the feasibility and effectiveness of such an adapted lifestyle intervention, tailored to the personal needs of each LS mutation carrier.

This is the first study investigating the effect of health promotion materials on awareness and knowledge of and adherence to lifestyle recommendations among LS mutation carriers, both shortly and longer after provision of these materials. However, our study had some limitations. LS mutation carriers already participating in the GeoLynch study were not invited for the current study. Since only 4% of LS mutation carriers eligible for invitation participated in the GeoLynch study, this is unlikely to have biased our results. Our study population consisted of a selected group of LS mutation carriers who agreed to participate in a study about lifestyle and cancer risk (response rate 53%). LS mutation carriers that were randomized were more likely to be older, female, and to have had a previous diagnosis of cancer compared to non-responders. Therefore, this may not be a representative sample of LS mutation carriers. Drop-out was higher in the control group than in the intervention group. However, data were missing at random and by using a mixed models analysis unbiased effect estimates were obtained.<sup>41</sup> The effects of the intervention on adherence and cancer worry at T1 may have been underestimated; the questionnaires referred to health behaviours and cancer worry in the last month, which also included the period of 2 weeks prior to the intervention. Timing of T1 at 2 weeks after the intervention was chosen best suitable for the primary outcome awareness, for which measurement shortly after the intervention was essential. Reliability of the questionnaire for awareness is acceptable (Cronbach's alpha .76 for T0, .83 for T1, and .80 for T2, but the questionnaire used for assessing knowledge has been self-developed and reliability is relatively poor (Cronbach's alpha 0.54 for T0, .74 for T1, and .57 for T2). Therefore, results for knowledge have to be interpreted with caution. Although all other measures have been routinely used in population-based epidemiologic and intervention research, the use of self-reported measures may have led to over-reporting (particularly physical activity) and under-reporting (particularly body weight).

Concluding, this study showed that the provision of WCRF-NL health promotion materials is an effective and easy-to-implement tool to increase awareness and knowledge of lifestyle recommendations for cancer prevention among LS mutation carriers, without causing

additional distress or cancer worry. Creating awareness is an important first step in increasing adherence to the recommendations for cancer prevention. As patient satisfaction and frequency of use of the provided WCRF-NL materials were high, this first-step approach could be easily included in a counseling or surveillance visit in the hospital. To actually increase adherence to the WCRF/AICR recommendations, lifestyle interventions should be developed that are adapted to the needs of LS mutation carriers.

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## Conflict of interest

The authors have declared no conflicting interests.

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#### SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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